

FILE 'USPAT' ENTERED AT 13:47:52 ON 31 JUL 1998

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*
*      W E L C O M E   T O   T H E
*      U . S .   P A T E N T   T E X T   F I L E
*
```

=> s collagen(la)(matrix or gel# or implant#)

11664 COLLAGEN
148931 MATRIX
163494 GEL#
23366 IMPLANT#

L1 988 COLLAGEN(1A)(MATRIX OR GEL# OR IMPLANT#)

=> s (BONE(W)MORPHOGEN?) or BMP? or (OSTEOGENIC(W)(PROTEIN? OR POLYPEPTIDE?))

31219 BONE
876 MORPHOGEN?
431 BONE(W)MORPHOGEN?
672 BMP?
659 OSTEOGENIC
78334 PROTEIN?
17867 POLYPEPTIDE?
93 OSTEOGENIC(W)(PROTEIN? OR POLYPEPTIDE?)

L2 834 (BONE(W)MORPHOGEN?) OR BMP? OR (OSTEOGENIC(W)(PROTEIN? OR P

OLY

PEPTIDE?))

=> s TGFbeta## or (TGF(W)BETA##) or ((TRANSFORMING(W)GROWTH(W)FACTOR#)(1A)beta##)

3 TGFbeta##
1598 TGF
170609 BETA##
1030 TGF(W)BETA##
27776 TRANSFORMING
137791 GROWTH
415655 FACTOR#
170609 BETA##
741 (TRANSFORMING(W)GROWTH(W)FACTOR#)(1A)BETA##

L3 1255 TGFbeta## OR (TGF(W)BETA##) OR ((TRANSFORMING(W)GROWTH(W)FA

CTO

R#)(1A)BETA##)

=> s l1 and l2

L4 101 L1 AND L2

=> s l1(p)l2

L5 21 L1(P)L2

=> s binding or binder

101283 BINDING
92565 BINDER
178310 BINDING OR BINDER

L6

=> s l5(p)l6

L7 0 L5(P)L6

=> s viscous or viscosity

84386 VISCOUS
175038 VISCOSITY
217752 VISCOUS OR VISCOSITY

L8

=> s l5 and l8

L9 9 L5 AND L8

=> s ?cellulose

<-----User Break----->

L10 144531 ?CELLULOSE

=>

u

=>

=>

YOU HAVE RECEIVED 3 CONSECUTIVE ARROW PROMPTS (=>)

The arrow (=>) is the system prompt, where you enter a command.

If you need an explanation of system commands, files, formats, etc., enter HELP and the name of the item you want explained at an arrow prompt (=>). The '?' can be used as a synonym for HELP at any prompt. Enter HELP COMMANDS for a list of commands that can be used in this file. Enter HELP MESSAGES for a list of online explanations that are available.

Help is available at any prompt, and after any error message.

Enter HELP or '?' at a prompt to see an explanation of the options.

After an error message, enter HELP or '?' at the next prompt and you will receive a more detailed explanation of the error and how to correct it.

Automatic help is also available. To turn off the automatic help feature, enter SET AUHELP NONE at an arrow prompt. When the SET parameter AUHELP is ON, you will automatically receive help following an error message. To receive automatic help after 2 consecutive error messages or 3 consecutive prompts, enter SET AUTOHELP OFF. For more information on the SET parameter AUHELP, enter HELP SET AUHELP at the arrow prompt (=>).

For a list of commands, enter HELP COMMANDS. For a list of online explanations, enter HELP MESSAGES.

IF YOU REQUIRE FURTHER HELP, PLEASE CONTACT YOUR LOCAL HELP DESK

=> d his

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(FILE 'USPAT' ENTERED AT 13:47:52 ON 31 JUL 1998)
L1      988 S COLLAGEN(1A) (MATRIX OR GEL# OR IMPLANT#)
L2      834 S (BONE(W)MORPHOGEN?) OR BMP? OR (OSTEOGENIC(W) (PROTEIN? O
R P
L3      1255 S TGF BETA## OR (TGF(W)BETA##) OR ((TRANSFORMING(W)GROWTH(W
)FA
L4      101 S L1 AND L2
L5      21 S L1(P)L2
L6      178310 S BINDING OR BINDER
L7      0 S L5(P)L6
L8      217752 S VISCOUS OR VISCOSITY
L9      9 S L5 AND L8
L10     144531 S ?CELLULOSE
```

=> s 15(p)?cellulose

```
144531 ?CELLULOSE
L11     0 L5(P)?CELLULOSE
```

=> s 15(p) (?cellulose or cellulosic)

```
144531 ?CELLULOSE
21781 CELLULOSIC
L12     0 L5(P) (?CELLULOSE OR CELLULOSIC)
```

=> s 15(2p) (?cellulose or cellulosic)

```
144531 ?CELLULOSE
21781 CELLULOSIC
L13     1 L5(2P) (?CELLULOSE OR CELLULOSIC)
```

=> d 1-

1. 5,645,591, Jul. 8, 1997, Synthetic bone matrix; Thangavel Kuberasampath, et al., 623/16, 66 [IMAGE AVAILABLE]

=> select]

ENTER ANSWER SET L#, TERMSET L# or (L13):end

=> select

ENTER ANSWER SET L#, TERMSET L# or (L13):l13

ENTER ANSWER NUMBER OR RANGE (1-):1

ENTER DISPLAY FORMAT (TI) OR ?:pn

E1 THROUGH E1 ASSIGNED

=> s e1

```
L14     1 "5,645,591"/PN
        (5645591/PN)
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=> d his

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(FILE 'USPAT' ENTERED AT 13:47:52 ON 31 JUL 1998)
L1      988 S COLLAGEN(1A) (MATRIX OR GEL# OR IMPLANT#)
L2      834 S (BONE(W)MORPHOGEN?) OR BMP? OR (OSTEOGENIC(W) (PROTEIN? O
R P
L3      1255 S TGF BETA## OR (TGF(W)BETA##) OR ((TRANSFORMING(W)GROWTH(W
)FA
L4      101 S L1 AND L2
L5      21 S L1(P)L2
L6      178310 S BINDING OR BINDER
L7      0 S L5(P)L6
L8      217752 S VISCOUS OR VISCOSITY
L9      9 S L5 AND L8
L10     144531 S ?CELLULOSE
L11     0 S L5(P)?CELLULOSE
L12     0 S L5(P) (?CELLULOSE OR CELLULOSIC)
```

L13 1 S L5(2P) (?CELLULOSE OR CELLULOSIC)
 SELECT

L13 1 PN

L14 1 S E1

=> s l14 and (collagen(2p) (?CELLULOSE OR CELLULOSIC))

11664 COLLAGEN
 144531 ?CELLULOSE
 21781 CELLULOSIC
 2529 COLLAGEN(2P) (?CELLULOSE OR CELLULOSIC)

L15 1 L14 AND (COLLAGEN(2P) (?CELLULOSE OR CELLULOSIC))

=> d kwic

US PAT NO: **5,645,591** [IMAGE AVAILABLE] L15: 1 of 1

SUMMARY:

BSUM(15)

The **collagen**-GAG polymer is cross-linked to control the solubility and mechanical properties of the matrix. It has been determined that cross-linking the. . .

SUMMARY:

BSUM(16)

The invention is embodied as a method of growing bone by conduction including contacting a viable mammalian bone with the cross-linked **collagen**-GAG matrix. Bone conduction is the growth of bone from existing viable bone, and involves the migration of osteoblasts from the. . . to solidify the matrix when implanted in a mammal or when placed at 37.degree. C. A useful glue is methyl **cellulose**. The matrix solidifies substantially in the shape of the implanted matrix.

SUMMARY:

BSUM(18)

Another . . . of producing the osteogenic device which contains osteogenic protein. The method includes providing a porous matrix comprising a polymer of **collagen** and GAG cross-linked to an M.sub.c value of about 800 to about 60,000; and dispersing within the matrix an osteogenic. . .

DETD(28)

Alternatively, . . . cobalt, or polymers such as polyglycolic acid or polylactic acid. Upon the addition of a heat-activated glue such as methyl **cellulose**, the material becomes solidified after implantation or when placed at 37.degree. C.

DETD(29)

Thus, . . . and cell division. Hence, osteoblasts may be induced to migrate from viable bone to the material. In addition, the cross-linked **collagen**-GAG material has a negative surface charge which enhances cell attachment. Furthermore, osteoblasts synthesize fibronectin, a cellular adherence protein that binds **collagen**, thereby enhancing the ability of the migrating osteoblasts to adhere to the implant.

DETD(31)

The . . . also comprise a molded, porous solid, or simply an aggregation of close-packed particles held in place by surrounding tissue. Insoluble **collagen** or inert polymers added to the **collagen**-GAG-osteogenic protein particles may increase the density of the device. In addition, a glue or solidifying agent including methyl **cellulose**, (e.g., Methocel, Dow Chemical Co.), may be added. It is preferable to shape the matrix into the desired form of. . .

DETD(32)

The . . . and evaluated histologically for evidence of bone formation. FIG. 1 demonstrates that only mesenchymal cells will be associated with a **collagen**-GAG implant that does not include osteogenic protein, while FIG. 2 shows the ultimate development of endochondral bone in an implant. . .

CLAIMS:

CLMS(10)

10. The method of claim 9 wherein said glue comprises methyl
cellulose.

CLAIMS:

CLMS(11)

11. . . . method of growing mammalian bone by conduction comprising
the steps of:

(A) providing a porous matrix comprising a polymer of **collagen** and
glycosaminoglycan cross-linked to an Mc value of about 800 to about
60,000 and a glue comprising methyl **cellulose** in an amount
sufficient to solidify said matrix when implanted in a mammal; and
(b) contacting viable mammalian bone at the. . .

=> d bib date ab

US PAT NO: **5,645,591** [IMAGE AVAILABLE] L15: 1 of 1
DATE ISSUED: Jul. 8, 1997
TITLE: Synthetic bone matrix
INVENTOR: Thangavel Kuberasampath, Medway, MA
Lawrence Berlowitz Tarrant, Harvard, MA
ASSIGNEE: Stryker Corporation, Natick, MA (U.S. corp.)
APPL-NO: 07/529,852
DATE FILED: May 29, 1990
ART-UNIT: 338
PRIM-EXMR: David Isabella
LEGAL-REP: Testa, Hurwitz & Thibault

L15: 1 of 1

TITLE: Synthetic bone matrix
US PAT NO: **5,645,591** DATE ISSUED: Jul. 8, 1997
[IMAGE AVAILABLE]
APPL-NO: 07/529,852 DATE FILED: May 29, 1990

ABSTRACT:

Disclosed is an osteogenic device capable of inducing the formation of
endochondral bone in a shape conforming substantially to the shape of the
device when implanted in a mammalian host. The device includes an
osteogenic protein dispersed within a porous matrix comprising a polymer
of collagen and glycosaminoglycan cross-linked to an M.sub.c value of
about 800 to about 60,000. Also disclosed are a method of inducing
mammalian bone growth, and a method of inducing conductive bone growth
from viable mammalian bone.

=> d his

(FILE 'USPAT' ENTERED AT 13:47:52 ON 31 JUL 1998)

L1 988 S COLLAGEN(1A) (MATRIX OR GEL# OR IMPLANT#)
L2 834 S (BONE(W)MORPHOGEN?) OR BMP? OR (OSTEOGENIC(W) (PROTEIN? O
R P
L3 1255 S TGFbeta## OR (TGF(W)BETA##) OR ((TRANSFORMING(W)GROWTH(W
)FA
L4 101 S L1 AND L2
L5 21 S L1(P)L2
L6 178310 S BINDING OR BINDER
L7 0 S L5(P)L6
L8 217752 S VISCOUS OR VISCOSITY
L9 9 S L5 AND L8
L10 144531 S ?CELLULOSE
L11 0 S L5(P)?CELLULOSE
L12 0 S L5(P) (?CELLULOSE OR CELLULOSIC)
L13 1 S L5(2P) (?CELLULOSE OR CELLULOSIC)
SELECT
L13 1 PN
L14 1 S E1
L15 1 S L14 AND (COLLAGEN(2P) (?CELLULOSE OR CELLULOSIC))

=> d bib date ab 1- 19

US PAT NO: 5,550,188 [IMAGE AVAILABLE] L9: 1 of 9
DATE ISSUED: Aug. 27, 1996
TITLE: Polymer conjugates ophthalmic devices comprising
collagen-polymer conjugates
INVENTOR: Woonza Rhee, Palo Alto, CA
Donald G. Wallace, Menlo Park, CA
Alan S. Michaels, Boston, MA
Ramon A. Burns, Jr., Fremont, CA
Louis Fries, Los Altos, CA
Frank DeLustro, Belmont, CA
Hanne Bentz, Newark, CA
ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
APPL-NO: 08/478,510
DATE FILED: Jun. 7, 1995
ART-UNIT: 127
PRIM-EXMR: Nathan M. Nutter
LEGAL-REP: Morrison & Foerster

TITLE: Polymer conjugates ophthalmic devices comprising collagen-polymer conjugates
 US PAT NO: 5,550,188 DATE ISSUED: Aug. 27, 1996
 [IMAGE AVAILABLE]
 APPL-NO: 08/478,510 DATE FILED: Jun. 7, 1995
 REL-US-DATA: Division of Ser. No. 368,874, Jan. 5, 1995, Pat. No. 5,446,051, which is a division of Ser. No. 198,128, Feb. 17, 1994, Pat. No. 5,413,791, which is a division of Ser. No. 922,541, Jul. 30, 1992, Pat. No. 5,328,955, which is a continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

ABSTRACT:
 Pharmaceutically acceptable, non-immunogenic compositions are formed by covalently binding atelopeptide collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, type II or type III and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The compositions may include other components such as liquid, pharmaceutically acceptable, carriers to form injectable formulations, and/or biologically active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amounts of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more.

US PAT NO: 5,475,052 [IMAGE AVAILABLE]
 DATE ISSUED: Dec. 12, 1995
 TITLE: Collagen-synthetic polymer matrices prepared using a multiple step reaction
 INVENTOR: Woonza M. Rhee, Palo Alto, CA
 Richard A. Berg, Los Altos, CA
 ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
 APPL-NO: 08/236,769
 DATE FILED: May 2, 1994
 ART-UNIT: 127
 PRIM-EXMR: Nathan M. Nutter
 LEGAL-REP: Kathi Rafayko

TITLE: Collagen-synthetic polymer matrices prepared using a multiple step reaction
 US PAT NO: 5,475,052 DATE ISSUED: Dec. 12, 1995
 [IMAGE AVAILABLE]
 APPL-NO: 08/236,769 DATE FILED: May 2, 1994
 REL-US-DATA: Continuation-in-part of Ser. No. 198,128, Feb. 17, 1994, which is a division of Ser. No. 922,541, Jul. 30, 1992, Pat. No. 5,328,955, which is a continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, Nov. 10, 1992, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

ABSTRACT:
 The present invention discloses collagen-synthetic polymer matrices which are prepared using a multiple step reaction. The first step of the reaction generally involves reacting collagen with a functionally activated synthetic hydrophilic polymer to form a collagen-synthetic polymer matrix. The synthetic hydrophilic polymer may be mono- or multifunctionally activated, but is preferably difunctionally activated, resulting in the formation of a crosslinked collagen matrix. The second step comprises modifying the collagen-synthetic polymer matrix according to one or more of the following methods: further crosslinking the matrix using a multifunctionally activated synthetic polymer, conjugating the matrix using a monofunctionally activated synthetic polymer, coupling biologically active molecules or glycosaminoglycans to the matrix, crosslinking the matrix using conventional chemical crosslinking agents, or modifying the collagen in the matrix by means of various chemical reactions. An optional third step may include further modification of the collagen-synthetic polymer matrix by covalently binding, for example, biologically active molecules or glycosaminoglycans to the matrix by means of available active groups on the synthetic hydrophilic polymers. Collagen-synthetic polymer matrices prepared according to the methods of the present invention have very low immunogenicity and can therefore be used to prepare biocompatible implants for use in a variety of medical applications.

US PAT NO: 5,446,091 [IMAGE AVAILABLE]
 DATE ISSUED: Aug. 29, 1995
 TITLE: Collagen-polymer conjugates containing an ether linkage
 INVENTOR: Woonza Rhee, Palo Alto, CA
 Donald G. Wallace, Menlo Park, CA
 Alan S. Michaels, Boston, MA
 Ramon A. Burns, Jr., Fremont, CA

Louis Fries, Los Altos, CA
Frank DeLustro, Belmont, CA
Hanne Bentz, Newark, CA
ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
APPL-NO: 08/368,874
DATE FILED: Jan. 5, 1995
ART-UNIT: 153
PRIM-EXMR: Nathan M. Nutter
LEGAL-REP: Morrison & Foerster

L9: 3 of 9

TITLE: Collagen-polymer conjugates containing an ether linkage
US PAT NO: 5,446,091 DATE ISSUED: Aug. 29, 1995
[IMAGE AVAILABLE]
APPL-NO: 08/368,874 DATE FILED: Jan. 5, 1995
REL-US-DATA: Division of Ser. No. 198,128, Feb. 17, 1994, Pat. No. 5,413,791, which is a division of Ser. No. 922,541, Jun. 30, 1992, Pat. No. 5,328,955, Jul. 12, 1994, which is a continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, Nov. 10, 1992, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

ABSTRACT:

Pharmaceutically acceptable, non-immunogenic compositions are formed by covalently binding atelopeptide collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, type II or type III and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The compositions may include other components such as liquid, pharmaceutically acceptable, carriers to form injectable formulations, and/or biologically active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amounts of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more.

US PAT NO: 5,413,989 [IMAGE AVAILABLE] L9: 4 of 9
DATE ISSUED: May 9, 1995
TITLE: Method and activin compositions for inducing bone growth
INVENTOR: Yasushi Ogawa, Pacifica, CA
David K. Schmidt, Santa Cruz, CA
Rosa Armstrong, Palo Alto, CA
Ranga Nathan, Newark, CA
Andrea Y. Thompson, Mountain View, CA
Saeid M. Seyedin, Saratoga, CA
ASSIGNEE: Celtrix Pharmaceuticals, Inc., Santa Clara, CA (U.S. corp.)
APPL-NO: 08/056,469
DATE FILED: May 3, 1993
ART-UNIT: 181
PRIM-EXMR: Jill A. Warden
ASST-EXMR: Carol A. Salata
LEGAL-REP: Morrison & Foerster

L9: 4 of 9

TITLE: Method and activin compositions for inducing bone growth
US PAT NO: 5,413,989 DATE ISSUED: May 9, 1995
[IMAGE AVAILABLE] DISCL-DATE: May 4, 2010
APPL-NO: 08/056,469 DATE FILED: May 3, 1993
REL-US-DATA: Continuation of Ser. No. 655,313, Feb. 14, 1991, Pat. No. 5,208,219.

ABSTRACT:

Activin is administered systemically and locally to induce the growth of mature bone. Activin enhances the level of bone formation and the quality of the bone formed when administered locally with BMP or bone marrow. Administration of activin by subcutaneous route promotes systemic increase in the bone mass.

US PAT NO: 5,413,791 [IMAGE AVAILABLE] L9: 5 of 9
DATE ISSUED: May 9, 1995
TITLE: Collagen-polymer conjugates
INVENTOR: Woonza Rhee, Palo Alto, CA
Donald G. Wallace, Menlo Park, CA
Alan S. Michaels, Boston, MA
Ramon A. Burns, Jr., Fremont, CA
Louis Fries, Los Altos, CA
Frank DeLustro, Belmont, CA
Hanne Bentz, Newark, CA
ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
APPL-NO: 08/198,128
DATE FILED: Feb. 17, 1994
ART-UNIT: 153
PRIM-EXMR: Nathan M. Nutter
LEGAL-REP: Morrison & Foerster

L9: 5 of 9

TITLE: Collagen-polymer conjugates
 US PAT NO: 5,413,791 DATE ISSUED: May 9, 1995
 [IMAGE AVAILABLE]
 APPL-NO: 08/198,128 DATE FILED: Feb. 17, 1994
 REL-US-DATA: Division of Ser. No. 922,541, Jul. 30, 1992, Pat. No. 5,328,955, which is a continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

ABSTRACT:
 Pharmaceutically acceptable, non-immunogenic compositions are formed by covalently binding atelopeptide collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, type II or type III and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The compositions may include other components such as liquid, pharmaceutically acceptable, carriers to form injectable formulations, and/or biologically active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amounts of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more.

L9: 6 of 9

US PAT NO: 5,328,955 [IMAGE AVAILABLE]
 DATE ISSUED: Jul. 12, 1994
 TITLE: Collagen-polymer conjugates
 INVENTOR: Woonza Rhee, Palo Alto, CA
 Donald G. Wallace, Menlo Park, CA
 Alan S. Michaels, Boston, MA
 Ramon A. Burns, Jr., Fremont, CA
 Louis Fries, Los Altos, CA
 Frank DeLustro, Belmont, CA
 Hanne Bentz, Newark, CA
 ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
 APPL-NO: 07/922,541
 DATE FILED: Jul. 30, 1992
 ART-UNIT: 153
 PRIM-EXMR: Nathan M. Nutter
 LEGAL-REP: Karl Bozicevic

L9: 6 of 9

TITLE: Collagen-polymer conjugates
 US PAT NO: 5,328,955 DATE ISSUED: Jul. 12, 1994
 [IMAGE AVAILABLE]
 APPL-NO: 07/922,541 DATE FILED: Jul. 30, 1992
 REL-US-DATA: Continuation-in-part of Ser. No. 433,441, Nov. 14, 1989, Pat. No. 5,162,430, which is a continuation-in-part of Ser. No. 274,071, Nov. 21, 1988, abandoned.

ABSTRACT:
 Pharmaceutically acceptable, non-immunogenic compositions are formed by covalently binding atelopeptide collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugates. The atelopeptide collagen can be type I, type II or type III and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The compositions may include other components such as liquid, pharmaceutically acceptable, carriers to form injectable formulations, and/or biologically active proteins such as growth factors. The collagen-polymer conjugates of the invention generally contain large amounts of water when formed. The conjugates can be dehydrated to form a relatively solid object. The dehydrated, solid object can be ground into particles which can be suspended in a non-aqueous fluid such as an oil and injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the particles rehydrate and expand in size five fold or more.

L9: 7 of 9

US PAT NO: 5,308,889 [IMAGE AVAILABLE]
 DATE ISSUED: May 3, 1994
 TITLE: Dehydrated collagen-polymer strings
 INVENTOR: Woonza Rhee, Pal Alto, CA
 Louis Fries, Los Altos, CA
 Ramesh Damani, Mountain View, CA
 Kimberly McCullough, Hayward, CA
 Frank DeLustro, Belmont, CA
 ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
 APPL-NO: 07/984,197
 DATE FILED: Dec. 2, 1992
 ART-UNIT: 153
 PRIM-EXMR: Nathan M. Nutter
 LEGAL-REP: Karl Bozicevic

L9: 7 of 9
TITLE: Dehydrated collagen-polymer strings
US PAT NO: 5,308,889 DATE ISSUED: May 3, 1994
[IMAGE AVAILABLE]
APPL-NO: 07/984,197 DATE FILED: Dec. 2, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 922,541, Jul. 30, 1992,
which is a continuation-in-part of Ser. No. 433,441,
Nov. 14, 1989, Pat. No. 5,162,430, Nov. 10, 1992, which
is a continuation-in-part of Ser. No. 274,071, Nov. 21,
1988, abandoned.

ABSTRACT:
Medical articles in the form of strings are formed by covalently binding collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugate formulations which are extruded to make the strings. The collagen may be recombinantly produced human collagen or collagen extracted from any source, such as a bovine source or human placenta, and purified and can be of various types and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having an average molecular weight over a range of from about 100 to about 20,000. The string can be designed to incorporate other components such as fluid, pharmaceutically acceptable carriers to form injectable formulations, and/or biologically active proteins such as growth factors or cytokines. The strings contain large amounts of water when extruded and may then be dehydrated to form relatively solid but flexible strings. The strings can be injected into a living being for the purpose of providing soft tissue augmentation. Once in place, the strings rehydrate and expand in size five fold or more. Aqueous solution can be provided to enhance the rate of rehydration. The strings can also be used to suture wounds which strings can be chemically designed to dissolve in situ.

US PAT NO: 5,292,802 [IMAGE AVAILABLE] L9: 8 of 9
DATE ISSUED: Mar. 8, 1994
TITLE: Collagen-polymer tubes for use in vascular surgery
INVENTOR: Woonza Rhee, Palo Alto, CA
Kimberly McCullough, Hayward, CA
ASSIGNEE: Collagen Corporation, Palo Alto, CA (U.S. corp.)
APPL-NO: 07/985,680
DATE FILED: Dec. 2, 1992
ART-UNIT: 153
PRIM-EXMR: Nathan M. Nutter
LEGAL-REP: Karl Bozicevic

L9: 8 of 9
TITLE: Collagen-polymer tubes for use in vascular surgery
US PAT NO: 5,292,802 DATE ISSUED: Mar. 8, 1994
[IMAGE AVAILABLE]
APPL-NO: 07/985,680 DATE FILED: Dec. 2, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 922,541, Jul. 30, 1992,
which is a continuation-in-part of Ser. No. 433,441,
Nov. 14, 1989, Pat. No. 5,162,430, Nov. 10, 1992, which
is a continuation-in-part of Ser. No. 274,071, Nov. 21,
1988, abandoned.

ABSTRACT:
Medical articles in the form of tubes are formed by covalently binding collagen to pharmaceutically pure, synthetic, hydrophilic polymers via specific types of chemical bonds to provide collagen/polymer conjugate formulations which are used to make the tubes. The collagen may be recombinantly produced human collagen or collagen extracted from any source, such as a bovine or human placental source, and purified and can be type I, type II or type III and may be fibrillar or non-fibrillar. The synthetic hydrophilic polymer may be polyethylene glycol and derivatives thereof having a weight average molecular weight over a range of from about 100 to about 20,000. The tube can be designed to incorporate other components such as liquid, pharmaceutically acceptable, carriers, and/or biologically active proteins such as growth factors or cytokines. The tubes contain large amounts of water when extruded and then may be dehydrated to form relatively solid but flexible tubes which can be easily stored. The tubes can be surgically implanted and attached to, or implanted within, a channel in a mammal for the purpose of repairing the channel. The tubes can be used to repair a wide range of different types of channels including but not limited to veins and arteries.

US PAT NO: 5,208,219 [IMAGE AVAILABLE] L9: 9 of 9
DATE ISSUED: May 4, 1993
TITLE: Method for inducing bone growth
INVENTOR: Yasushi Ogawa, Pacifica, CA
David K. Schmidt, Santa Cruz, CA
Rosa Armstrong, Palo Alto, CA
Ranga Nathan, Newark, CA
Andrea Y. Thompson, Mountain View, CA
Saeid M. Seyedin, Saratoga, CA
ASSIGNEE: Celtrix Pharmaceuticals Inc., Santa Clara, CA (U.S. corp.)
APPL-NO: 07/655,313
DATE FILED: Feb. 14, 1991
ART-UNIT: 181
PRIM-EXMR: F. T. Moezie
LEGAL-REP: Morrison & Foerster

L9: 9 of 9
TITLE: Method for inducing bone growth
US PAT NO: 5,208,219 DATE ISSUED: May 4, 1993
[IMAGE AVAILABLE]
APPL-NO: 07/655,313 DATE FILED: Feb. 14, 1991

ABSTRACT:
Activin is administered systemically and locally to induce the growth of mature bone. Activin enhances the level of bone formation and the quality of the bone formed when administered locally with BMP or bone marrow. Administration of activin by subcutaneous route promotes systemic increase in the bone mass.

=> save all a08822186/1

'A08822186/L' IN USE
REPLACE OLD DEFINITION? Y/(N):n

=> append all a08822186/1

'APPEND' IS NOT A RECOGNIZED COMMAND

=> act a08822186/1

L16 (19488)SEA FILE=USPAT ((OSTEOGENIC OR (BONE MORPHOGENETIC)) (W)PRO
TEI
L17 (11949)SEA FILE=USPAT COLLAGEN?
L18 (188)SEA FILE=USPAT DEMINERALIZED BONE
L19 (4637)SEA FILE=USPAT ?APATITE OR ?APATITES
L20 (138488)SEA FILE=USPAT PHOSPHATE?
L21 (87)SEA FILE=USPAT L17 (P) L18
L22 (19)SEA FILE=USPAT L21 (P) L19
L23 (3)SEA FILE=USPAT L22(P)L20
L24 (2)SEA FILE=USPAT L23 AND L16
L25 (20323)SEA FILE=USPAT MANNITOL
L26 (12895)SEA FILE=USPAT DEXTRAN OR DEXTRANS
L27 (1214)SEA FILE=USPAT WHITE PETROLATUM
L28 (6784)SEA FILE=USPAT SESAME OIL
L29 (4052)SEA FILE=USPAT CELLULOSES
L30 (14013)SEA FILE=USPAT L26 OR L27
L31 (1214)SEA FILE=USPAT L27(P)L30
L32 (31221)SEA FILE=USPAT L25 OR L26
L33 (29)SEA FILE=USPAT L27(P)L32
L34 (1068)SEA FILE=USPAT L28(P)L32
L35 (481)SEA FILE=USPAT L29(P)L32
L36 (0)SEA FILE=USPAT L33(P)L28
L37 (0)SEA FILE=USPAT L33(P)L29
L38 (47)SEA FILE=USPAT L16 AND (L33 OR L34 OR L35)

=> d his

(FILE 'USPAT' ENTERED AT 13:47:52 ON 31 JUL 1998)
L1 988 S COLLAGEN(1A) (MATRIX OR GEL# OR IMPLANT#)
L2 834 S (BONE(W)MORPHOGEN?) OR BMP? OR (OSTEOGENIC(W) (PROTEIN? O
R P
L3 1255 S TGF BETA## OR (TGF(W)BETA##) OR ((TRANSFORMING(W)GROWTH(W
)FA
L4 101 S L1 AND L2
L5 21 S L1(P)L2
L6 178310 S BINDING OR BINDER
L7 0 S L5(P)L6
L8 217752 S VISCOUS OR VISCOSITY
L9 9 S L5 AND L8
L10 144531 S ?CELLULOSE
L11 0 S L5(P)?CELLULOSE
L12 0 S L5(P) (?CELLULOSE OR CELLULOSIC)
L13 1 S L5(2P) (?CELLULOSE OR CELLULOSIC)
SELECT
L13 1 PN
L14 1 S E1
L15 1 S L14 AND (COLLAGEN(2P) (?CELLULOSE OR CELLULOSIC))
ACT A08822186/L

L16 (19488)SEA FILE=USPAT ((OSTEOGENIC OR (BONE MORPHOGENETIC)) (W)PRO
TEI
L17 (11949)SEA FILE=USPAT COLLAGEN?
L18 (188)SEA FILE=USPAT DEMINERALIZED BONE
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